Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 17-23 stand rejected because, according to the Office, the specification does not enable any person skilled in the art to which the specification pertains to make and use the invention commensurate in scope with these claims. Specifically, the Office contends that the specification does not teach a screening method that differentiates between (1) neutralizing antibodies and (2) antibodies that bind EPO epitopes that bind the EPO receptor, and thus does not demonstrate a mechanism whereby the binding of neutralizing antibodies to EPO would not bind epitopes of EPO that are responsible for receptor binding. The Office further asserts that Sytkowski et al. (*J. Biol. Chem.* 262:1161-65 1987; "Sytkowski") suggest that their peptides, 99-118 and 111-129, represent the receptor binding domain of EPO and therefore the neutralizing activity of these antibodies is due to interference with the binding of EPO with its receptor. Applicants respectfully traverse the Office's rejection for the following reasons.

First, antibodies that neutralize EPO activity do not necessarily bind to EPO epitopes that bind the EPO receptor. The specification need not demonstrate these alternative mechanisms because they are well known to those of ordinary skill in the art. For example, Sytkowski discusses two other possible alternative explanations for how neutralizing antibodies may work. In one instance, these antibodies may inhibit EPO activity not by binding the receptor epitopes on EPO, but by binding near them and sterically inhibiting or physically blocking the interaction of EPO with its receptor. In another instance, neutralizing antibodies may bind nowhere near the receptor domain on EPO, but many nonetheless inhibit EPO function by causing an allosteric

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

change in the hormone molecule. Thus, just because an antibody is neutralizing does not necessarily mean that it targets receptor binding domains on EPO.

Second, Applicants respectfully assert that the Office has not interpreted Sytkowski correctly. Though Sytkowski did suggest in the abstract that the EPO 99-118 and 111-129 peptides *probably* form part of the EPO receptor binding domain, Sytkowski goes on to clearly show that in fact these peptides do not directly bind the EPO receptor. Applicants note that in doing so, Sytkowski employed methods commonly known to those of ordinary skill in the art that did not require undue experimentation. Specifically, Sytkowski reported that the six peptides used to generate their antibodies failed to demonstrate any EPO biological activity and that these peptides failed to inhibit the biological activity of whole EPO. More importantly, these authors directly state that "none of these peptides react[s] directly with the erythropoietin receptor" (p.1162, right column, first full paragraph). This is why Sytkowski considers alternative mechanisms by which antibodies to these peptides may be working, as discussed above. Thus, Sytkowski's results clearly distinguish the antibodies disclosed in this reference from the claimed antibodies that specifically bind EPO epitopes that bind to the EPO receptor. Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 5-7, 9-12, and 14-16 stand rejected as being indefinite for allegedly failing to distinctly claim the subject matter regarded as the invention. Specifically, the Office refers to the phrase, "consists essentially of" and requests clarification as to how this phrase relates to the

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& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
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terms "consists of" and "comprises."

Applicants respectfully assert that the phrase "consists essentially of" is a term of the art. In addressing how claims using the phrase "consisting essentially of" are construed, the Federal Circuit noted that:

> By using the term "consisting essentially of," the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A "consisting essentially of" claim occupies a middle ground between closed claims that are written in a "consisting of" format and fully open claims that are drafted in a "comprising" format.

P.P.G. Indus. v. Guardian Indus., Corp., 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998). When the court's reasoning is applied to the instant invention, independent claim 5 necessarily includes EPO peptides P4, P1/1, P5, P5/1, P2, and P2/1 and any unlisted ingredients that do not materially affect the usage of these peptides in preparing epitope-specific anti-EPO antibodies. This includes, for example, the addition of a small number of amino acids onto either end of the EPO peptide, such that the new peptide still generates epitope-specific anti-EPO antibodies. Likewise, when the court's reasoning is applied to independent claim 6, this claim necessarily includes EPO peptides P2 and P2/1 and any unlisted ingredients that do not materially affect the ability of the claimed neutralizing antibodies to recognize these peptides. Thus, as currently written, independent claims 5 and 6 do distinctly claim the invention. Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Rejection Under 35 U.S.C. § 102(b)

Claims 17 and 18 stand rejected as allegedly anticipated by Sytkowski. Specifically, the Office asserts that claims 17 and 18 are drawn to an anti-EPO antibody directed against an EPO epitope that binds the EPO receptor. According to the Office, Sytkowski recites two antibodies that were able to neutralize EPO activity. As stated by the Office in its 35 U.S.C. § 112, First Paragraph rejection above, the specification is allegedly not enabling for discerning between neutralizing antibodies and antibodies that bind to EPO epitopes that bind the EPO receptor. Thus, according to the Examiner, Sytkowski discloses all the embodiments of claims 17 and 18. Applicants respectfully traverse the Office's rejection for the following reasons.

Applicants note that, as the specification provides at page 3, the "intention [of the invention] is furthermore to provide novel EPO peptides which bind to the EPO receptor [and] . . . to provide antibodies against said EPO peptides . . . ." This spirit of the invention was subsequently embodied in independent claim 17, which recites "an anti-erythropoietin (EPO) antibody directed against epitopes that bind to the EPO receptor." As discussed on page 3 of this response, Sytkowski's peptides clearly do not bind to the EPO receptor. Therefore, Sytkowski's antibodies, directed to peptides that do not bind the EPO receptor, cannot anticipate the claimed invention.

In conclusion, for the reasons discussed above, the Office's rejection of claims 17 and 18 does not satisfy the legal standards for anticipation. Applicants therefore respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(b).

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000

Conclusion

Applicants respectfully request that this Response be entered by the Office, placing claims 5-7, 9-12, and 14-23 in condition for allowance.

In view of the foregoing remarks, Applicants submit that their claimed invention is not anticipated in view of the prior art reference cited against this application. Applicants therefore respectfully request the entry of this Response, the Office's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any additional extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: Carol P. Einaudi.
Carol P. Einaudi
Reg. No. 32,220

Date: July 10, 2001

LAW OFFICES
FINNEGAN, HENDERSON,
FARABOW, GARRETT,
& DUNNER, L.L.P.
1300 I STREET, N. W.
WASHINGTON, DC 20005
202-408-4000